REMARKS

The amendments to the specification correct obvious grammatical errors and do not add new matter. The amendments to claims 50-54, 59, 68, 74, 75-79 and 109-99 also correct obvious errors and clarify the language used. These amendments do not add new matter and do not change the scope of the claims. For example, the terms "alkaline cation" and "alkaline earth cations" have been amended to clarify that the cations are alkali and alkaline earth metal cations, respectively. Support for "trifluoromethane sulfonic acid" is found on page 6, line 16.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Page 1, line 1, after the title insert

--Priority is claimed to provisional application Serial No. 60/367,380, filed on January 12, 2001.--

Paragraph beginning at page 4, line 24, has been amended as follows:

wherein Q is -O-, -S-, $-N(R^7)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a_2-$, $-S-(CH_2)_m-$, and $-N(R^7)(CH_2)_m-$, where m= 1-3, and X^a is halogen; and

Paragraph beginning at page 6, line 13, has been amended as follows:

The present invention is also directed to pharmaceutically acceptable salts of formula I. Suitable pharmaceutically acceptable salts are well known to those skilled in the art and include basic salts of inorganic and organic acids, such as hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, ~~methanesulphonic~~ methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, *p*-toluenesulfonic acid, 1-naphthalenesulfonic acid, 2-naphthalenesulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid. In addition, pharmaceutically acceptable salts include acid salts of inorganic bases, such as salts containing alkaline cations (e.g., Li^+ Na^+ or K^+), alkaline earth cations (e.g., Mg^{+2}, Ca^{+2} or Ba^{+2}), the ammonium cation, as well as acid salts of organic bases, including aliphatic and aromatic substituted ammonium, and quaternary ammonium cations, such as those arising from protonation or peralkylation of triethylamine, *N,N*-diethylamine, *N,N*-dicyclohexylamine, lysine, pyridine, *N,N*-dimethylaminopyridine (DMAP), 1,4-diazabiclo[2.2.2]octane (DABCO), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

Paragraph beginning at page 13, line 22, has been amended as follows:

It will be appreciated by those skilled in the art that the particular method of administration will depend on a variety of factors, all of which are considered routinely when administering therapeutics. It will also be appreciated by one skilled in the art that the specific dose level for a given patient depends on a variety of factors, including specific activity of the compound administered, age, body weight, health, sex, diet, time and route of administration, rate of excretion, etc. It will be further appreciated by one skilled in the art that the optimal course of treatment, ~~ie.~~ i.e., the mode of treatment and the daily number of doses of a compound of Formula I or a pharmaceutically acceptable salt thereof given for a defined number of days, can be ascertained by those skilled in the art using conventional treatment tests.

Paragraph beginning at page 14, line 8, has been amended as follows:

The entire ~~enclosure~~ disclosure of all applications, patents and publications cited above and below are hereby incorporated by reference, including provisional application Serial No. 60/115,877, filed January 13, 1999 and non-provisional application Serial No. 09/257,266 filed February 25, 1999.

Paragraph beginning at page 24, line 16, has been amended as follows:

Step 3. Synthesis of 5-(4-aminophenoxy)isoindoline-1,3-dione

A solution of 5-(4-nitrophenoxy)isoindoline-1,3-dione (0.6 g, 2.11 mmol) in conc. AcOH (12 mL) and water (0.1 mL) was stirred under a stream of argon while iron powder (0.59 g, 55.9 mmol) was added slowly. This mixture stirred at room temp. for 72 h, then was diluted with water (25 mL) and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to give 5-(4-aminophenoxy)isoindoline-1,3-dione as a brownish solid (0.4 g, 75%): TLC (50% EtOAc/50% hexane) R_f 0.27; ^{1}H NMR (DMSO-d_6) δ 5.14 (br s, 2H), 6.62 (d, J=8.7 Hz, 2H), 6.84 (d, J=8.7 Hz, 2H), 7.03 (d, J=2.1 Hz, 1H), 7.23 (dd, 1H), 7.75 (d, J=8.4 Hz, 1H), 11.02 (s, 1H); HPLC ES-MS *m/z* 255 ($(M+H)^+$, 100%).

Paragraph beginning at page 26, line 22, has been amended as follows:

A6. General Method for the Synthesis of Anilines from Hydroxyanilines by *N*-Protection, Nucleophilic ~~Aromatic~~ Aromatic Substitution and Deprotection. Synthesis of 4-(2-(*N*-Methylcarbamoyl)-4-pyridyloxy)-2-chloroaniline

Paragraph beginning at page 29, lines 2, has been amended as follows:

A8. General Method for Synthesis of ω-Alkoxy-ω-carboxyphenyl Anilines. Synthesis of 4-(3-(~~*N*-Methylcarbamoly~~ *N*-Methylcarbamoyl)-4-methoxyphenoxy)aniline.

Paragraph beginning at page 29, line 23, has been amended as follows:

Step 3. 4-(3-(~~*N*-Methylcarbamoly~~ *N*-Methylcarbamoyl)-4-methoxyphenoxy)-1-nitrobenzene:

Paragraph beginning at page 30, line 9, has been amended as follows:

To a solution of 4-(3-carboxy-4-methoxyphenoxy)-1-nitrobenzene (0.50 g, 1.75 mmol) in CH_2Cl_2 (12 mL) was added $SOCl_2$ (0.64 mL, 8.77 mmol) in portions. The resulting solution was heated at the reflux temp. for 18 h, cooled to room temp., and concentrated under reduced pressure. The resulting yellow solids were dissolved in CH_2Cl_2 (3 mL) then the resulting solution was treated with a methylamine solution (2.0 M in THF, 3.5 mL, 7.02 mmol) in portions (CAUTION: gas evolution), and stirred at room temp. for 4 h. The resulting mixture was treated with a 1N NaOH solution, then extracted with CH_2Cl_2 (25 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give 4-(3-(~~*N*-methylcarbamoly~~ *N*-methylcarbamoyl)-4-methoxyphenoxy)-1-nitrobenzene as a yellow solid (0.50 g, 95%).

Paragraph beginning at page 30, line 12, has been amended as follows:

Step 4. 4-(3-(~~*N*-Methylcarbamoly~~ *N*-Methylcarbamoyl)-4-methoxyphenoxy)aniline: A slurry of 4-(3-(*N*-methylcarbamoly)-4-methoxyphenoxy)-1-nitrobenzene (0.78 g, 2.60 mmol) and 10% Pd/C (0.20 g) in EtOH (55 mL) was stirred under 1 atm of H_2 (balloon) for 2.5 d, then was filtered through a pad of Celite®. The resulting solution was concentrated under reduced pressure to afford 4-(3-(*N*-methylcarbamoly)-4-methoxyphenoxy)aniline as an off-white solid (0.68 g, 96%): TLC (0.1% Et_3N/99.9% EtOAc) R_f 0.36.

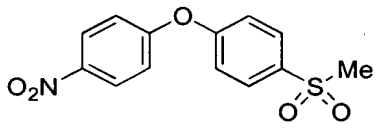
Paragraph beginning at page 34, line 10, has been amended as follows:

Step 2. Synthesis of 4-(1-isoindolinon-5-yloxy)-1-nitrobenzene

To a slurry of NaH (0.39 g, 16.1 mmol) in DMF at 0 °C was added 5-hydroxyisoindolin-1-one (2.0 g, 13.4 mmol) in portions. The resulting slurry was allowed to warm to room temp. and was stirred for 45 min., then 4-fluoro-1-nitrobenzene was added and then the mixture was heated at 70 °C for 3 h. The mixture was cooled to 0 °C and treated with water dropwise until a precipitate formed. The resulting solids were collected to give 4-(1-isoindolinon-5-yloxy)-1-nitrobenzene as a dark yellow solid (3.23 g, 89%): TLC (100% EtOAc) R_f 0.35.

Paragraph beginning at page 42, line 15, has been amended as follows:

A19. Synthesis of ω-Sulfonylphenyl Anilines. Synthesis of 4-(4-~~Methylsulfonylphenyoxy~~ Methylsulfonylphenoxy)aniline.



Step 1. 4-(4-Methylsulfonylphenoxy)-1-nitrobenzene: To a solution of 4-(4-methylthiophenoxy)-1-nitrobenzene (2.0 g, 7.7 mmol) in CH_2Cl_2 (75 mL) at 0 °C was slowly added *m*-CPBA (57-86%, 4.0 g), and the reaction mixture was stirred at room temperature for 5 h. The reaction mixture was treated with a 1N NaOH solution (25 mL). The organic layer was sequentially washed with a 1N

NaOH solution (25 mL), water (25 mL) and a saturated NaCl solution (25 mL), dried ($MgSO_4$), and concentrated under reduced pressure to give 4-(4-methylsulfonylphenoxy)-1-nitrobenzene as a solid (2.1 g).

Paragraph beginning at page 50, line 13, has been amended as follows:

C3. Combinatorial Method for the Synthesis of Diphenyl Ureas Using Triphosgene

One of the anilines to be coupled was dissolved in dichloroethane (0.10 M). This solution was added to a 8 mL vial (0.5 mL) containing dichloroethane (1 mL). To this was added a bis(trichloromethyl) carbonate solution (0.12 M in dichloroethane, 0.2 mL, 0.4 equiv.), followed by diisopropylethylamine (0.35 M in dichloroethane, 0.2 mL, 1.2 equiv.). The vial was capped and ~~heat~~ heated at 80 °C for 5 h, then allowed to cool to room temp for approximately 10 h. The second aniline was added (0.10 M in dichloroethane, 0.5 mL, 1.0 equiv.), followed by diisopropylethylamine (0.35 M in dichloroethane, 0.2 mL, 1.2 equiv.). The resulting mixture was heated at 80 °C for 4 h, cooled to room temperature and treated with MeOH (0.5 mL). The resulting mixture was concentrated under reduced pressure and the products were purified by reverse phase HPLC.

Paragraph beginning at page 52, line 2, has been amended as follows:

D. Interconversion of Ureas

D1a. Conversion of ω-Aminophenyl Ureas into ω-(~~Aroylamino~~ Arylamino)phenyl Ureas. Synthesis of *N*-(4-Chloro-3-((trifluoromethyl)phenyl)-*N'*-(4-(3-methoxycarbonylphenyl)carboxyaminophenyl) Urea

Paragraph beginning at page 59, line 25, has been amended as follows:

Entry 15: According to Method C2d, 5-(~~triflouromethyl~~ trifluoromethyl)-2-methoxyaniline was reacted with CDI followed by 4-(3-*N*-methylcarbamoyl)-4-methoxyphenoxy)aniline, which had been prepared according to Method A8, to afford the urea.

IN THE CLAIMS:

Claims 50-59, 68, 74, 75-79 and 99 have been amended as follows.

Claim 50. (Twice Amended) A pharmaceutically acceptable salt of claim 69 ~~selected from the group consisting of~~ which is

a) a basic salt ~~salts~~ of an organic acid ~~acids and~~ or an inorganic acid ~~acids selected from the group consisting of~~ which is hydrochloric acid, hydrobromic acid, ~~sulphuric~~ sulfuric acid, phosphoric acid, ~~methanesulphonic~~ methanesulfonic acid, ~~trifluorosulphonic~~ trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene ~~sulphonic~~ sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, ~~and~~ or mandelic acid; ~~and~~ or

b) an acid salt ~~salts~~ of an organic ~~and~~ or inorganic base ~~bases~~ containing ~~cations selected from the group consisting of~~ an ~~alkaline cations~~ alkali metal cation, an alkaline earth metal cation ~~cations~~, ~~the~~ an ammonium cation, an aliphatic substituted ammonium cation ~~cations and~~ or an aromatic substituted ammonium cation ~~cations~~.

Claim 51. (Twice Amended) A pharmaceutically acceptable salt of claim 70 ~~selected from the group consisting of~~ which is

a) a basic salt ~~salts~~ of an organic acid ~~acids and~~ or an inorganic acid ~~acids selected from the group consisting of~~ which is hydrochloric acid, hydrobromic acid, ~~sulphuric~~ sulfuric acid, phosphoric acid, ~~methanesulphonic~~ methanesulfonic acid, ~~trifluorosulphonic~~ trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene ~~sulphonic~~ sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, ~~and~~ or mandelic acid; ~~and~~ or

b) an acid salt ~~salts~~ of an organic ~~and~~ or inorganic base ~~bases~~ containing ~~cations selected from the group consisting of alkaline cations~~ an alkali metal cation, an alkaline earth metal

cation ~~cations~~, ~~the~~ an ammonium cation, an aliphatic substituted ammonium cation ~~cations and~~ or an aromatic substituted ammonium ~~cations~~ cation.

Claim 52. (Twice Amended) A pharmaceutically acceptable salt of claim 71 ~~selected from the group consisting of~~ which is

a) a basic ~~salts~~ salt of an organic acid ~~acids and~~ or an inorganic acid ~~acids selected from the group consisting of~~ which is hydrochloric acid, hydrobromic acid, ~~sulphuric~~ sulfuric acid, phosphoric acid, ~~methanesulphonic~~ methanesulfonic acid, ~~trifluorosulphonic~~ trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene ~~sulphonic~~ sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, ~~and~~ or mandelic acid; ~~and~~ or

b) an acid salt ~~salts~~ of an organic ~~and~~ or inorganic base ~~bases~~ containing ~~cations selected from the group consisting of alkaline cations~~ an alkali metal cation, an alkaline earth metal cation ~~cations~~, ~~the~~ an ammonium cation, an aliphatic substituted ammonium cation ~~cations and~~ or an aromatic substituted ammonium cation ~~cations~~.

Claim 53. (Twice Amended) A pharmaceutically acceptable salt of claim 72 ~~selected from the group consisting of~~ which is

a) a basic salt ~~salts~~ of an organic acid ~~acids and~~ or inorganic acid ~~acids selected from the group consisting of~~ which is hydrochloric acid, hydrobromic acid, ~~sulphuric~~ sulfuric acid, phosphoric acid, ~~methanesulphonic~~ methanesulfonic acid, ~~trifluorosulphonic~~ trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene ~~sulphonic~~ sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, ~~and~~ or mandelic acid; ~~and~~ or

b) an acid salt ~~salts~~ of an organic ~~and~~ or inorganic base ~~bases~~ containing ~~cations selected from the group consisting of alkaline cations~~ an alkali metal cation, an alkaline

earth metal cation ~~cations~~, ~~the~~ an ammonium cation, an aliphatic substituted ammonium cation ~~cations and~~ or an aromatic substituted ammonium cation ~~cations~~.

Claim 54. (Twice Amended) A pharmaceutically acceptable salt of claim 73 ~~selected from the group consisting of~~ which is

a) a basic salt ~~salts~~ of organic acid ~~acids and~~ or an inorganic acid ~~acids selected from the group consisting of~~ which is hydrochloric acid, hydrobromic acid, ~~sulphuric~~ sulfuric acid, phosphoric acid, ~~methanesulphonic~~ methanesulfonic acid, ~~trifluorosulphonic~~ trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene ~~sulphonic~~ sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, ~~and~~ or mandelic acid; ~~and~~ or

b) an acid salts of an organic ~~and~~ or inorganic base ~~bases~~ containing ~~cations selected from the group consisting of alkaline cations~~ an alkali metal cation, an alkaline earth metal cation ~~cations~~, ~~the~~ an ammonium cation, an aliphatic substituted ammonium cation ~~cations and~~ or an aromatic substituted ammonium cation ~~cations~~.

68. (Amended) A pharmaceutically acceptable salt of a compound ~~selected from the group consisting of~~ which is:

N-(5-*tert*-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea; or

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea ~~and their pharmaceutically acceptable salts~~.

74. (Amended) A method for the treatment of a cancerous cell growth mediated by ~~RAF~~ raf kinase comprising administering a pharmaceutically acceptable salt of ~~a compound~~ which is ~~selected from the group consisting of~~:

N-(5-*tert*-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea; or

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

75. (Amended) A method for the treatment of a cancerous cell growth as in claim 74 ~~mediated by RAF kinase~~ comprising administering a pharmaceutically acceptable salt of

N-(5-tert-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methyl carbamoyl)phenoxy)phenyl) urea.

76. (Amended) A method for the treatment of a cancerous cell growth as in claim 74 ~~mediated by RAF kinase~~ comprising administering a pharmaceutically acceptable salt of

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

77. (Amended) A method for the treatment of a cancerous cell growth as in claim 74 ~~mediated by RAF kinase~~ comprising administering a pharmaceutically acceptable salt of

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea.

78. (Amended) A method for the treatment of a cancerous cell growth as in claim 74 ~~mediated by RAF kinase~~ comprising administering a pharmaceutically acceptable salt of

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

79. (Amended) A method for the treatment of a cancerous cell growth as in claim 74 ~~mediated by RAF kinase~~ comprising administering a pharmaceutically acceptable salt of

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

99. (Amended) A method as in claim 74 wherein the pharmaceutically acceptable salt ~~administered~~ is ~~selected from the group of salts consisting of~~

a) a basic salt ~~salts~~ of an organic acid ~~acids and~~ or an inorganic acid ~~acids selected from the group consisting of~~ which is hydrochloric acid, hydrobromic acid, ~~sulphuric~~ sulfuric acid, phosphoric acid, ~~methanesulphonic~~ methanesulfonic acid, ~~trifluorosulphonic~~ trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene ~~sulphonic~~ sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, ~~and~~ or mandelic acid; ~~and~~ or

b) an acid salt ~~salts~~ of an organic ~~and~~ or inorganic base ~~bases~~ containing ~~cations selected from the group consisting of~~ an alkali metal cation ~~alkaline cations~~, an alkaline earth metal cation ~~cations~~, ~~the~~ an ammonium cation, an aliphatic substituted ammonium cation ~~cations and~~ or an aromatic substituted ammonium cation ~~cations~~.

100. (Amended) A method as in claim 75 wherein ~~where~~ the pharmaceutically ~~pharmaceutical~~ acceptable salt administered is the tosylate salt of

N-(5-tert-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methyl carbamoyl)phenoxy)phenyl) urea.

101. (Amended) A method as in claim 76 wherein ~~where~~ the pharmaceutically ~~pharmaceutical~~ acceptable salt administered is the tosylate salt of

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

102. (Amended) A method as in claim 77 wherein ~~where~~ the pharmaceutically ~~pharmaceutical~~ acceptable salt administered is the tosylate salt of

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea.

103. (Amended) A method as in claim 78 wherein ~~where~~ the pharmaceutically ~~pharmaceutical~~ acceptable salt administered is the tosylate salt of

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

104. (Amended) A method as in claim 79 wherein ~~where~~ the pharmaceutically ~~pharmaceutical~~ acceptable salt administered is the tosylate salt of

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

105. (Amended) A pharmaceutically ~~pharmaceutical~~ acceptable salt as in claim 69 which is the tosylate salt of

N-(5-*tert*-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea.

106. (Amended) A pharmaceutically ~~pharmaceutical~~ acceptable salt as in claim 70 which is the tosylate salt of

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

107. (Amended) A pharmaceutically ~~pharmaceutical~~ acceptable salt as in claim 71 which is the tosylate salt of

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea.

108. (Amended) A pharmaceutically ~~pharmaceutical~~ acceptable salt as in claim 72 which is the tosylate salt of

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

109. (Amended) A pharmaceutically ~~pharmaceutical~~ acceptable salt as in claim 73 which is the tosylate salt of

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.